

**REMARKS**

The Office Action and the cited and applied references have been carefully studied. No claim is allowed. Claims 1-4, 14-15, and 21-22 presently appear in the application and define patentable subject matter warranting their allowance. Reconsideration and allowance are hereby respectfully solicited.

Claims 5-20 have been rejected under 35 U.S.C. §112, second paragraph, as being indefinite. This rejection is obviated by the amendments to the claims.

Claims 5-7 and 15-17 have been rejected under 35 U.S.C. §101 because the examiner holds that the claimed recitation of use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. §101. Claims 5 and 15 are amended, thereby obviating this rejection.

Claims 1-20 have been rejected under 35 U.S.C. §102(b) as being anticipated by or, in the alternative, under 35 U.S.C. 103(a) as being obvious over Grigoriadis et al. The examiner states that Grigoriadis teaches a mesenchymal cell line which can differentiate into diverse cell types and also discloses factors which cause such differentiation. It is the

examiner's position that the applied reference anticipates the claimed subject matter.

The examiner holds that although the instant cell line is defined as being "derived from a normal adult", the application does not demonstrate any difference between the cell line claimed and that disclosed in the prior art nor does it provide any factual evidence whatsoever to refute the holding of anticipation. This rejection is respectfully traversed.

The RCJ 3.1 cell line of Grigoriadis is derived from mesenchymal cells of fetal rat calvaria. By contrast, the cell line according to the present invention is derived from a "normal adult animal", which is defined in the specification on page 9 to exclude embryo-derived cells. In a preferred embodiment of the present invention, the cell line is derived from mesenchymal cells of the crural bones of a normal adult animal. Accordingly, the RCJ 3.1 cell line of Grigoriadis cannot anticipate the presently claimed invention.

Furthermore, as evidence that the cell line of the present invention is different from fetal or embryonic cell lines, it should be noted that the RCJ 3.1 cell line of Grigoriadis is disclosed as not differentiating into adipocytes unless dexamethasone was added to the culture medium (page 2142, right column, lines 1-11 of lower paragraph

(adipocyte formation)). Grigoriadis also disclosed that nodules appeared only when R3.1 cells were treated with dexamethasone (page 2144, left column, lower paragraph on cartilage formation). Therefore, it is clear that the R3.1 cells of Grigoriadis require dexamethasone to differentiate into adipocytes or chondrocytes. By contrast, the cell line according to the present invention, as exemplified in Example 2, differentiates into adipocyte or chondrocytes in the absence of dexamethasone.

Additional evidence of the difference between fetal or embryonic cell lines and adult cell lines are as follows:

1. Koike et al., J. Clin. Invest. 85:626-631 (1990), a copy of which is attached hereto, report that although parathyroid hormone (PTH) stimulated the proliferation of chondrocytes derived from embryonic animals, it did not stimulate the proliferation of chondrocytes derived from postnatal 3 week old animals (see abstract and Fig. 6).

2. Also attached hereto is a declaration executed by Hidetomo Kitamura, the inventor of the present invention. The results, obtained from an experiment conducted by applicant according to method similar to that described by Koike et al., demonstrate that PTH did not stimulate the proliferation of cell line CL-1, which cell line is derived from a normal adult animal.

1. Hoike et al. and the results obtained by applicant indicate that cell response against information transmission substances, such as hormones, differs depending on the source of the animal from which the cells are derived. Accordingly, the presently claimed invention cannot be made obvious from Grigoriadis.

Claims 10-13 and 19-20 are now canceled without prejudice, thereby obviating the rejection as it relates to rejected claims 10-13 and 19-20.

Reconsideration and withdrawal of the rejection are therefore respectfully requested.

Claims 1-3 and 5-20 have been rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This rejection is respectfully traversed.

The present specification at page 9 discloses that the cells from which the cell lines according to the present invention are derived are selected from crural bones, femoral bones, cranial bones, tracheae, auricles, nose, intervertebral disks, or heart. It is submitted that such disclosed sources of cells are adequate written description for the cell lines

and that the present invention because specifically identified sources, from which cell lines can be readily obtained, are described by applicant. Furthermore, cells from these specific sources can be readily determined as to whether or not such cells differentiate into chondrocytes (see pages 10-11 of the specification) or adipocytes (see pages 11-12 of the specification).

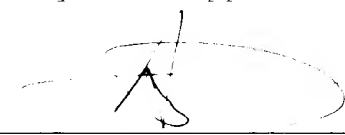
Reconsideration and withdrawal of the rejection are therefore respectfully requested.

In view of the above, the claims comply with 35 U.S.C. §112 and define patentable subject matter warranting their allowance. Favorable consideration and early allowance are earnestly urged.

Respectfully submitted,

BROWDY AND NEIMARK, P.L.L.C.  
Attorneys for Applicant(s)

By

  
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Allen C. Yun  
Registration No. 37,971

ACY:pr  
Telephone No.: (202) 628-5197  
Facsimile No.: (202) 737-3528

VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the claims:

Claims 1, 4, 9, 8, 15, and 18 have been amended as follows:

1 (Twice-amended). A cell line capable of differentiating into chondrocytes and capable of differentiating into adipocytes, which cell is derived from a normal adult animal.

4 (Twice-amended). The cell line of ~~claim 1~~ claim 21, which bears accession No. FERM BP-5823.

5 (Twice-amended). A method for screening for a cell differentiation-controlling material, comprising: using  
contacting a compound or a mixture of compounds with  
the cell line of claim 1 to screen for a cell differentiation-  
controlling material; and  
determining the capability of the compound or the  
mixture of compounds to induce differentiation of the cell  
line.

8 (Twice-amended). A kit for screening for a cell differentiation-controlling material, comprising the cell line

claim 1 and a reagent for detecting changes of properties of the cell line which may be caused by the action of a candidate cell differentiation-controlling material to be screened.

15(Once-amended). A method for screening for a cell differentiation-controlling material, comprising: using  
contacting a compound or a mixture of compounds with the cell line of claim 14 to screen for a cell differentiation-controlling material; and  
determining the capability of the compound or the mixture of compounds to induce differentiation of the cell line.

18(Once-amended). A kit for screening for a cell differentiation-controlling material, comprising the cell line of claim 4 and a reagent for detecting changes of properties of the cell line which may be caused by the action of a candidate cell differentiation-controlling material to be screened.